



Tunable biomimetic systems based on a novel amphiphilic pyrimidinophane and a helper nonionic surfactant

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ABSTRACT

Tunable nanosystems based on a novel water insoluble pyrimidinic amphiphile are designed. pH dependent aggregates composed of protonated pyrimidinophane **1** are formed at pH < 4, which undergo reversible transition to precipitate at neutral and basic conditions. The approach assuming the application of a helper nonionic surfactant Triton-X-100 (**TX-100**) is used in this work. Different models of a self-assembly were found depending on the molar ratio of components and solution pH. In the equimolar **1** – **TX-100** solution, mixed assemblies contributed by aggregated molecules of both **TX-100** and cationic form of **1** are formed in acidic conditions. Upon alkalization, deprotonated pyrimidinophane molecules shift toward the micellar core. The assemblies undergo reversible precipitation after 4–5 h, while the excess of **TX-100** leads to the formation of highly stable mixed aggregates. The acidification–alkalization cycles followed by the aggregation/precipitation and the re-charging of aggregates can be multiply repeated. Surprisingly, stable mixed aggregates are also formed under the excess of pyrimidinophane in both the acidic and alkaline conditions, but at a certain component ratio. They are characterized by the highest micellization degree among all the systems studied. The low concentration threshold of these assemblies in alkali solution is probably due to their nonionic character.

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1. Introduction

One of the most promising strategies of the design of modern high-effective systems is a “bottom-up” approach [1], which can be particularly based on a non-covalent self-assembly of amphiphiles. Such a controllable self-organization has a great potential in biotechnologies, where soft and smart systems are applied, e.g. fine-tuned drug and gene delivery supramolecular nanocontainers, biomimetic nanoreactors with adjustable reactivity features, etc. [2–7]. The nature of building blocks for such ensembles determines their properties. Therefore some key criteria should be followed, when amphiphile compounds are chosen, e.g. low concentrations in order to avoid toxic effects and expenses, biocompatibility, stimuli responsibility, controllability of self-organization processes, etc.

Among the desirable systems, cationic nanocontainers are of special interest. They exhibit the affinity for such important

biological polyanions as DNA and can be applied for the transport of biosubstrates or drugs through the negatively charged cell membranes [8–11]. In our works, we focus on the construction of such kind of nanocontainers with tunable surface properties, morphology, and solubilization ability [12–15]. Herein, new supramolecular ensembles based on the pyrimidinocyclophane **1** (Scheme 1) with an uracil moiety are described. It is common knowledge that uracils are the constituents of nucleic acids and other biologically important molecules [16,17]. Uracils are capable of self-assembling through different mechanisms: van der Waals, hydrogen-bonding, etc. This makes the systems with uracil and its 5(6)-substituted derivatives good candidates for the role of building blocks for the development of nanocontainers for bioapplications [18–23]. Moreover, amphiphilic nature of **1** could give some additional advantages related to self-organization process.

It is of key importance in biomedical applications to design stable nanocontainers with cationic surface charge and low toxicity. A common way to develop lipid base formulations answering this criterion is the use of mixed liposomes composed of cationic amphiphile and helpers, e.g. zwitter-ionic lipids providing the aggregative stability to the system [24,25]. Taking this into account

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